Alternative activation of exracellular signal-regulated protein kinases in curcumin and arsenite induced HSP70 gene expression in human colorectal carcinoma cells

李婉若

Chen YC;Tsai SH;Shen SC and Lee WR

摘要

Abstract

We have investigated the regulation mechanism of chemical stress-induced HSP70 gene expression in human colorectal carcinoma cells (COLO205 and HT29). Our data show that chemical treatments including sodium arsenite and curcumin, induced significant synthesis of HSP70 and its mRNA. The induced HSP70 gene expression appears to be increased at the transcriptional level. The increase in HSP70 gene expression by both chemicals is associated with an increase in HSF binding to HSE and induction of HSF1 di- or trimerization. Phosphorylation and activation of extracellular signal-regulated proteins (ERK1/2) were detected in sodium arsenite-treated COLO205 and HT29 cells, and the free radical scavenger N-acetyl-L-cysteine (NAC) was able to inhibit this ERK1/2 activation and HSP70 gene expression. MAPK blockade by the specific MEK1 inhibitor (PD98059) decreased the ability of sodium arsenite to increase HSP70 gene expression in a dose-dependent manner along with dephosphorylation of ERK1/2 proteins. In contrast to arsenite treatment, activation of ERK1/2 was not detected in curcumin-treated colorectal carcinoma cells, and NAC and PD98059 did not show any inhibitory effect on HSP70 gene expression induced by curcumin. Overexpression of a dominant negative mutant of mitogen-activated protein kinase kinase kinase 1 (MEKK1-DN) prevents arsenite-induced ERK1/2 phosphorylation and HSP70 protein synthesis. These results indicated that the ERK signaling pathway can participate in HSP70 gene expression induced by the prooxidant sodium

arsenite, but not by the antioxidant curcumin.